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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,924	07/15/2003	Gopi Venkatesh	451194-095	7145

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THOMPSON HINE L.L.P.
Intellectual Property Group
P.O. BOX 8801
DAYTON, OH 45401-8801

EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

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12/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/619,924	VENKATESH ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

Claims 1-5, 7-27 and 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1, in view of Bins US 4,777,044.

Gantt teaches a process for preparing a controlled release potassium chloride (KCl) tablet comprising coating KCl particles with two coating layers by coacervation using polyethylene as a phase separator, blending the coated KCl particles with excipients, and then compressing the blended mixture into tablet (abstract; pages 3-4). First coating layer comprises ethyl cellulose having viscosity of about 90 to about 110 cp (page 3, 1st and 2nd paragraphs). Second coating layer comprises polyvinyl pyrrolidone, ethyl cellulose, hydroxypropylmethyl cellulose, or combination thereof (page 3, 3rd paragraph). Plasticizer such as triacetin, triethyl citrate, dibutyl sebacate, or PEG 400 is included in the second coating composition (page 3, 4th paragraph). Excipient includes binder, disintegrant (microcrystalline cellulose), wetting agent (surfactant), and lubricating agent (page 4, last paragraph through page 5, 1st paragraph).

Gantt does not explicitly teach the claimed silicon dioxide.

Bins teaches a dry compressed ammonium nitrate tablet comprising solid ammonium nitrate and tabletting auxiliary (abstract). Suitable tabletting auxiliary includes microcrystalline cellulose, colloidal silicon dioxide, and magnesium stearate (surfactant) (column 1, lines 60 through column 2, lines 1-7). Bins also teaches the claimed tablet hardness in the use of colloidal silicon dioxide, namely, tablet hardness of

at least 15 kP (column 2, lines 20-22). Bins also teaches the amount of microcrystalline cellulose is from 5%-50%, and the amount of colloidal silicon dioxide is from 0.05%-10% (column 2, lines 3-7).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the tablet composition of Gantt to include silicon dioxide as the tabletting auxiliary in view of the teachings of Bins, because Bins teaches using colloidal silicon dioxide in a compressed tablet formulation is well known in the art, because Bins teaches using colloidal silicon dioxide to obtain tablet hardness at a level that gives the best results when coated, because Bins teaches that suitable and acceptable tablet hardness is obtained in the use of colloidal silicon dioxide, and because Gantt teaches the use of pharmaceutically acceptable excipient suitable for compressed tablet.

Claims 1-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1, in view of Vilkov et al. US 5,807,579.

Gantt is relied upon for the reason stated above. Gantt does not teach using colloidal silicon dioxide, and the claimed plasticizing agent.

Vilkov teaches a pharmaceutical tablet composition for oral administration comprising an active agent, and suitable tablet excipients including talc, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate (surfactant). The tablet has a hardness of 9-17 kP (column 5, lines 60-67). Vilkov also teaches coating comprising plasticizing agent such as triethyl citrate and diethyl phthalate (column 4, lines 33-42).

Vilkov further teaches the amount of colloidal silicon dioxide (column 6, lines 3-13). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the tablet formulation of Gantt to include colloidal silicon dioxide as a tablet excipient, and diethyl phthalate as a plasticizing agent to obtain the claimed invention. This is because Vilkov teaches the equivalency of diethyl phthalate with other well known plasticizing agent, because Vilkov teaches using colloidal silicon dioxide is a well known tablet excipient, because Gantt teaches the use of tablet excipients, and because Gantt teaches the use of other plasticizing agents in the compressed tablet formulation.

Response to Arguments

Applicant's arguments filed 09/12/08 have been fully considered but they are not persuasive.

Applicant argues that the combination of Gantt and Bins or Gantt and Vilkov, fails to properly *support prima facie* obviousness because the combination lacks any disclosure of tablets having 0.3% friability as in the present claims. Specifically, Bins is silent on friability Values, and Gantt merely mentions that certain tablets have "low friability" without reporting values. The Examiner provides no other evidence or knowledge in the art suggesting the claimed friability, and even if, *arguendo,* Gantt's or Bins's or Vilkov's tablets inherently disclosed the claimed friability values, an obviousness rejection cannot be predicated on a property inherent or unknown at the time of the invention. MPEP § 2141.02. Applicants note that the friability of the claimed

tablets, and provided by the claimed process, affords improved tablet strength and resistance to abrasion and attrition during transport and storage.

However, in response to applicant's arguments regarding the friability, the burden is shifted to applicant to show that the tablet taught by Bins or Vilkov does not have the claimed friability. It is noted that Bins and Vilkov teach the use of microcrystalline cellulose and silicon dioxide in the claimed amounts. Bins and Vilkov further teach the use of silicon dioxide as an excipient for compressed tablet is well known in the art. Accordingly, one of ordinary skill in the art would have been motivated to modify the compressed tablet of Gantt to include silicon dioxide with the expectation to improve the tablet properties, such as tablet hardness.

Applicant argues that the Examiner uses an improper hindsight analysis by combing Gantt and Bins or Gantt and Vilkov to arrive at the claimed invention. Applicants' claimed tablet comprises a potassium chloride crystal surrounded by two distinct layers (an inner layer of ethylcellulose and an outer layer of plasticized polymer) to form a microcapsule. These microcapsules are mixed with microcrystalline cellulose and colloidal silicon dioxide, and the mixture is compressed into a tablet. The colloidal silicon dioxide provides superior hardness and friability properties compared to otherwise substantially identical tablets without colloidal silicon dioxide. Gantt also teaches controlled-release potassium chloride tablets, but Gantt's tablets do not contain colloidal silicon dioxide, as the Examiner acknowledged.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Further, in response to applicant's argument that Gantt does not teach tablets contain colloidal silicon dioxide, it is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Gantt is cited in view of Bins for the teachings of silicon dioxide.

Applicant argues that the Examiner relies on Bins or Vilkov to cure this deficiency in Gantt. Bins and Vilkov include colloidal silicon dioxide in the compression mixture of a compressed tablet of ammonium nitrate. Unlike Gantt, Bins's or Vilkov's tablet does not contain microcapsules, but rather an unstructured drug/excipient compression mix. The only polymeric layer taught in Bins coats the outside of the tablet. Bins's preferred tablet-coating polymers contain carboxylate moieties that immediately dissolve in the intestine and remain intact in the stomach. Bins and Gantt disclose numerous components in their respective tablets, allowing for numerous combinations, the vast

majority of which would not provide the claimed invention. For example, one skilled in the art could just as readily incorporate the potassium chloride crystals of Gantt directly into the compression mixture as taught by Bins, then singly coat the final tablet with Bins's preferred enteric polymer. Or the skilled artisan might choose the dual coating from Gantt's microcapsules and apply it outside the Bins-inspired tablet. In either case, the resulting combination would not provide the claimed tablet because neither combination would contain Gantt's dual-coated microcapsules. Since neither Bins nor Gantt provides sufficient direction to make the specific combination suggested by the Examiner, only the benefit of hindsight informed by Applicants' disclosure would reasonably prompt the Examiner's proposed modification to incorporate Bins's colloidal silicon dioxide into Gantt's compression mixture, while ignoring Bins's other preferred teachings (e.g., controlled-release coating on the outside of the tablet).

However, in response to applicant's argument that Bins or Vilkov does not teach tablets containing microcapsules but rather an unstructured drug/excipient, it is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Bins or Vilkov is cited solely for the teachings that silicon dioxide is a well known compressible excipient to improve compressed tablet properties.

Applicants note that these Bins or Vilkov inspired modifications to Gantt would be expected to sacrifice many of the benefits of the claimed invention. For instance, incorporating Gantt's potassium chloride crystals into Bins's tablet coated with an enteric polymer (i.e., swapping KCl for ammonium nitrate) would result in immediate release of potassium chloride as soon as the tablet entered into the intestine. This combination would provide a delayed, immediate release of potassium chloride, along with the well-known side effects of gastrointestinal irritation, purging, weakness, and circulatory disturbances. The second combination mentioned above (coating a Bins-styled tablet with the dual coating on Gantt's microcapsule) would reasonably be expected to result in localized release of potassium chloride in the intestine and cause gastric irritation.

In response to applicant's arguments, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As discussed above, Bins or Vilkov is cited solely for the teachings of the well known compressed tablet auxiliaries such as microcrystalline cellulose, potassium chloride, and magnesium stearate.

Applicant argues that Bins and Vilkov teaches the use of lubricant, therefore, teaches away from "substantially free of lubricant" as recited in the claims.

However, although "magnesium stearate" is known in the art as a lubricating agent, "magnesium stearate" is also known as a surfactant (see for example paragraph 0112 of the Xilinas reference).

Pertinent Arts

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kopf is cited as of interest for the teaching of potassium tablet comprising excipient such as colloidal silicon dioxide.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615